US PAT NO: 5,043,101 [IMAGE AVAILABLE] L7: 30 of 32

ABSTRACT:
This invention provides particle compositions possessing ferromagnetic, paramagnetic or diamagnetic properties. The particles are especially useful when used in the disease diagnostic and treatment regimens as described in U.S. Pat. Nos. 4,106,448, 4,136,683 and 4,303,636.

US PAT NO: 4,920,061 [IMAGE AVAILABLE] L7: 31 of 32

ABSTRACT:
Colloidal-sized **paramagnetic particles** are formed with affinity ligands directly adsorbed to their surface. The colloidal-sized particles can form a colloidal disperse phase which is distributed through an aqueous dispersion medium to form a biological magnetic fluid. The fluid can be used to selectively separate cells from a cell mixture.

US PAT NO: 4,735,796 [IMAGE AVAILABLE] L7: 32 of 32

ABSTRACT:
This invention provides particle compositions possessing ferromagnetic, paramagnetic or diamagnetic properties. The particles are especially useful when used in the disease diagnostic and treatment regimens as described in U.S. Pat. Nos. 4,106,448, 4,136,683 and 4,303,636.

=> d l7 kwic 30-32

US PAT NO: 5,043,101 [IMAGE AVAILABLE] L7: 30 of 32
TITLE: Ferromagnetic, diamagnetic or **paramagnetic particles** useful in the diagnosis and treatment of disease

SUMMARY:

BSUM(4)

The . . . frequency alternating electromagnetic field inductively heating the intracellular particles thus resulting in an increase in the intracellular temperature of the **cells**. Because the **cancer cells** accumulate the particles to a greater degree than the normal cells and further because of the higher ambient temperature of a **cancer cell** as compared to the normal cells; the temperature increase results in the death of the **cancer cells** but with little or no damage to normal cells in the treatment area. The particles are optionally used with specific **cancer cell** targeting materials (antibodies, radioisotopes and the like).

DETDESC:

DETD(3)

According to one form of the invention, selective treatment of **cancer cells** is achieved without damaging normal cells. The process comprises introducing minute particles into the interior of the cells of living. . . particles sufficiently to raise the temperature of the cells by an increment of 8.0.degree. to 9.5.degree. centigrade

thus killing the **cancer cells** without harming the normal cells. Further selectivity and increased affinity of the **cancer cells** for these particles may be achieved by incorporating specific radioisotopes or tumor specific antibodies bound to these particles.

DETDESC:

DETD(4)

When the ferromagnetic, diamagnetic or **paramagnetic particles** described above are employed as a cancer treating composition, the particle size of the particles should be not greater than. . .

DETDESC:

DETD(6)

Electronmicrographs of the cancerous tissue have proven the selective pickup of the magnetic particles by the **cancer cells**.

DETDESC:

DETD(7)

It . . . the intracellular temperature of the cells may be raised between 8.0.degree. centigrade and 9.5.degree. centigrade to cause death in the **cancer cell** without damage being caused to the normal cells.

DETDESC:

DETD(11)

In . . . intracellularly as described may be used as a method of delivering a chemotherapeutic agent primarily to the interior of the **cancer cells** by having the chemotherapeutic agent encapsulated within said particles and released at the proper time by application of the high. . .

DETDESC:

DETD(21)

Thus, . . . is, of course, predicated on the case situation in which particle distribution, magnetic state and orientation were equal in all **cancer cells** and normal **cells** under the treatment conditions. However, employing the improved methods of the subject invention thereby affecting specific particle distribution, orientation, differential magnetic susceptbility, timing and other parameters described herein, between the **cancer cells** and the normal cells within the target area, increases in the intracellular temperature up to 100.degree. C. are possible without. . .

DETDESC:

DETD(22)

Irreversible . . . death and biological alterations are induced by the energy input to the particle and thereupon to the interior of the **cancer cell**. Thus, the same energy input may be accomplished by application over a long period of time with a consistent small. . .

DETDESC:

DETD(31)

Further . . . where the Fe.sub.3 O.sub.4 is optionally substituted with a transition metal, rare earth metal, metalloporphyrin or other ferromagnetic, diamagnetic or **paramagnetic particle** wherein the **antibody** is of **monoclonal** or polyclonal origin and is specifically reactive to the specific target organ or cell-type desired.

DETDESC:

DETD(32)

Metallothionein-based . . . lectin is used in combination with Fe.sub.3 O.sub.4 or the transition metal, rare earth metal, metalloporphyrin and ferromagnetic, diamagnetic or **paramagnetic particles** as described above.

US PAT NO: 4,920,061 [IMAGE AVAILABLE] L7: 31 of 32

ABSTRACT:
Colloidal-sized **paramagnetic particles** are formed with affinity ligands directly adsorbed to their surface. The colloidal-sized particles can form a colloidal disperse phase which. . .

SUMMARY:

BSUM(1)

The . . . generally to magnetic colloidal liquids useful for biological and medical applications. More particularly, the invention is directed to novel colloidal-sized **paramagnetic particles** coated with biologically active molecules or affinity ligands. The particles are useful, for example, in allogenic bone marrow transplantation for. . .

SUMMARY:

BSUM(4)

When . . . is aspirated from patients in remission and cryopreserved. After the patient is treated with high dose chemotherapy to eliminate residual **cancer cells**, the marrow is thawed and reinfused to rescue the hematopoietic system which is eliminated by the high dose chemotherapy. This. . .

SUMMARY:

BSUM(5)

The advent of **monoclonal antibodies** has opened a new frontier for the characterization of cell surface antigens. By immunizing mice, removing the immune spleen cells. . . the identical antibodies can be utilized around the world. The potential for transplantation has been realized by many different groups. **Monoclonal antibodies** which react with the components on the surface of leukemic cells have been reported by several groups, and some groups have used **monoclonal antibody** treatment of bone marrow prior to transplantation.

SUMMARY:

BSUM(6)

Work has started on techniques for linking a **monoclonal antibody** to a boron containing compound. Diseased tissue, targeted by the antibody, may be exposed to a "slow" (thermal) neutron beam. . .

SUMMARY:

BSUM(7)

The . . . unwanted cells from a cell suspension has been studied by a large number of investigators. Particularly in the treatment of **cancer**, the removal of **cells** circumvents numerous problems involved in using toxins, chemotherapeutic agents and complement but has been limited to in vitro physical removal. Density gradient separations have been used to remove residual **cancer cells** from bone marrow cells, but these were not highly efficient.

SUMMARY:

BSUM(20)

Accordingly, in one embodiment, the present invention includes colloidal-sized **paramagnetic particles** of cobalt coated with affinity ligands. Advantageously, the colloidal-sized particles are at least greater than about 30 nanometers in diameter.. . .

DETDESC:

DETD(29)

The affinity ligands of biologically active macromolecules attached to the individual colloidal magnetic particles can bind **monoclonal** or polyclonal **antibodies** which attack and adhere to specific cells of biological interest, such as **cancer cells**. Because of the magnetic properties of the colloid, cell separations may be accomplished. For example, cancerous bone marrow cells may. . .

DETDESC:

DETD(32)

An . . . the strong binding nature of avidin and biotin. The avidin-biotin complex is essentially irreversible under most conditions. By using biotinylated **monoclonal antibodies** or biotinylated lectins, or other binding agents, which can selectively bind to certain cell types, avidin-coated colloidal cobalt particles can. . .

DETDESC:

DETD(33)

For example, it is anticipated that a "cocktail" of **monoclonal antibodies** which can be used for the magnetic removal of each acute leukemia cell type could be developed. Using both biotinylated. . .

DETDESC:

DETD(34)

High . . . a reducing agent can be used to coat selected cell populations from a mixture of cells in vitro (such as **cancer cells** in human bone marrow). The **cancer** or other **cells** can be selected by an appropriately specific **monoclonal antibody** adhered on the colloidal particles, as described above. After careful washing of the cells to remove excess (free) colloid, the. . . the colloid coated cells, while leaving the others viable and undamaged. In this way bone marrow can be purged of **cancer cells** or other **cells**. Because of the high density of dispersed boron atoms obtainable with the present invention, the probability of achieving a boron/neutron. . .

DETDESC:

DETD(64)

The . . . to remove granulocytes and red cells. To remove graft versus host disease causing cells, the cells are incubated with mouse **monoclonal antibody** (CT-2) for 45 minutes at 4.degree. C. which reacts with E-rosette receptor positive lymphocytes (T-cells). The CT-2 antibody, a pan T-cell **monoclonal antibody**, is described in the article by M. Trigg, R. Billing, et al., "In Vitro Treatment of Donor Bone Marrow with. . .

DETDESC:

DETD(67)

Monoclonal antibody-reactive cells that escape the separation procedure are detected in a variety of ways. Immunofluorescence may be used either with a. . .

DETDESC:

DETD(76)

A mononuclear cell fraction of bone marrow cells was incubated with a pool of **monoclonal antibodies**, OKT3 +OKT4+OKT8+OKT11, for 30 minutes a 4.degree. in PBS containing 2% fetal bovine serum (PBS-FBS). The cells were washed by. . .

US PAT NO: 4,735,796 [IMAGE AVAILABLE] L7: 32 of 32
TITLE: Ferromagnetic, diamagnetic or **paramagnetic particles** useful in the diagnosis and treatment of disease

SUMMARY:

BSUM(4)

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According to one form of the invention, selective treatment of **cancer cells** is achieved without damaging normal cells. The process comprises introducing minute particles into the interior of the cells of living. . . particles sufficiently to raise the temperature of the cells by an increment of 8.0.degree. to 9.5.degree. centigrade thus killing the **cancer cells** without harming the normal cells. Further selectivity and increased affinity of the **cancer cells** for these particles may be achieved by incorporating specific radioisotopes or tumor specific antibodies bound to these particles.

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DETD(6)

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DETDESC:

DETD(7)

It . . . the intracellular temperature of the cells may be raised between 8.0.degree. centigrade and 9.5.degree. centigrade to cause death in the **cancer cell** without damage being caused to the normal cells.

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DETD(11)

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DETD(21)

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Irreversible . . . death and biological alterations are induced by the energy input to the particle and thereupon to the interior of the **cancer cell**. Thus, the same energy input may be accomplished by application over a long period of time with a consistent small. . .

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DETD(31)

Further . . . where the Fe.sub.3 O.sub.4 is optionally substituted with a transition metal, rare earth metal, metalloporphyrin or other ferromagnetic, diamagnetic or **paramagnetic particle** wherein the **antibody** is of **monoclonal** or polyclonal origin and is specifically reactive to the specific target organ or cell-type desired.

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Metallothionein-based . . . lectin is used in combination with Fe.sub.3 O.sub.4 or the transition metal, rare earth metal, metalloporphyrin and ferromagnetic, diamagnetic or **paramagnetic particles** as described above.

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     (FILE 'USPAT' ENTERED AT 15:36:32 ON 13 MAY 1999)
L1           455 S PARAMAGNETIC (A) (PARTICLE? OR BEAD? OR MICROPARTICLE? O
R M
L2         18203 S (MURINE? OR HUMAN? OR MONOCLONAL?) (3A) ANTIBOD?
L3          8062 S (ONCOGEN? OR CANCER OR METASTA?) (3A) CELL?
L4          2205 S DETERGENT? AND (POLYETHYLENESORBITAN MOLAUREATE OR TWEEN
 20
L5           684 S DETERGENT? (P) (POLYETHYLENESORBITAN MOLAUREATE OR TWEEN
 20
L6           169 S L1 AND L2
L7            32 S L3 AND L6
L8             2 S L7 AND L5
L9            32 S L1 AND L2 AND L3
L10            8 S L9 AND L4
```

US PAT NO: 5,019,497 [IMAGE AVAILABLE] L8: 13 of 15
DATE ISSUED: May 28, 1991
TITLE: Human squamous lung carcinoma cell specific antigens and antibodies
INVENTOR: Lennart Olsson, Rigshospitalet 9, Blegdamsvej, Copenhagen, Denmark, DK-2100
APPL-NO: 07/215,056
DATE FILED: Jul. 5, 1988
ART-UNIT: 182
PRIM-EXMR: Esther L. Kepplinger
ASST-EXMR: Florima B. Hoffer
LEGAL-REP: Bertram I. Rowland

US PAT NO: 4,857,452 [IMAGE AVAILABLE] L8: 14 of 15
DATE ISSUED: Aug. 15, 1989
TITLE: Assay for carcinoma of breast, colon and ovary
INVENTOR: May-Kin Ho, Carlisle, MA
ASSIGNEE: E. I. Du Pont de Nemours and Company, Wilmington, DE (U.S. corp.)
APPL-NO: 06/937,771
DATE FILED: Dec. 4, 1986
ART-UNIT: 181
PRIM-EXMR: Christine M. Nucker
ASST-EXMR: D. John Griffith, Jr.

US PAT NO: 4,752,569 [IMAGE AVAILABLE] L8: 15 of 15
DATE ISSUED: Jun. 21, 1988
TITLE: Sialylated Lewis.sup.x epitope, antibodies and diagnosis
INVENTOR: Paul I. Terasaki, Los Angeles, CA
Masaki Hirota, Gardena, CA
Kiyoyasu Fukushima, Gardena, CA
Akemi Wakisaka, Torrance, CA
Takashi Iguro, Torrance, CA
ASSIGNEE: The Regents of the University of California, Berkeley, CA (U.S. corp.)
APPL-NO: 06/623,309
DATE FILED: Jun. 21, 1984
ART-UNIT: 128
PRIM-EXMR: Sidney Marantz
ASST-EXMR: David A. Saunders
LEGAL-REP: Bertram I. Rowland

US PAT NO: 5,019,497 [IMAGE AVAILABLE] L8: 13 of 15

ABSTRACT:
Methods and compositions are provided for detecting antigens having a specific epitope associated with squamous lung carcinoma. The antigen may be found at lesion sites or in the blood as indicative of the squamous lung carcinoma.
Specific antibodies may be used for the detection of the antigen and in therapy.
The mouse hybridoma 43-9F producing IgM monoclonal antibody 43-9F and SLC cell RH-SLC-L11 were deposited at The PHLS Centre for Applied Microbiology and Research, Porton Down, Salisbury, U.K. on Jan. 31, 1985 and given Accession Nos. 85013101 and 85061403, respectively.

US PAT NO: 4,857,452 [IMAGE AVAILABLE] L8: 14 of 15

ABSTRACT:
Colorectal, breast or ovarian cancer can be detected by means of a blood, plasma, serum, urine or feces assay for elevated levels of 47D10 antigen using a monoclonal antibody to the antigen.

US PAT NO: 4,752,569 [IMAGE AVAILABLE] L8: 15 of 15

ABSTRACT:
Detection of sialylated Lewis.sup.x antigen in sera is employed as diagnostic of the presence of cancer. Conveniently, monoclonal antibodies are provided which are shown to be useful in the diagnosis of a neoplastic condition, with a wide variety of different tumors.
The hybridoma CSLEX1 was deposited at the A.T.C.C. on June 20, 1984 and given Accession No. HB8580.

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US PAT NO: 5,019,497 [IMAGE AVAILABLE] L8: 13 of 15

SUMMARY:

BSUM(3)

Cancer cells synthesize unusual and sometimes highly specific proteins and glycolipids that in many cases have been identified as fetal or embryonic macromolecules apparently produced in the **cancer cell** after either aberrant activation or failure to deactivate genes normally silent in differentiated cells. Some of these gene-products may influence the abnormal proliferative properties of the **cancer cells**. Sensitive methods are needed for identifying the unusual cellular compounds with high tumor specificity, because they may provide signals for. . .

SUMMARY:

BSUM(6)

Olsson et al., Cancer (1984) 54:1757-1765 report monoclonal antibodies for lung carcinoma. Antisera and monoclonal antibodies with reactivity to human lung **cancer cells** have been described by Kelly and Levy,

Br. J. Cancer (1977) 35:828-833; Cuttita et al., Proc. Natl. Acad. Sci. USA. . . . of the subtypes of lung cancer: small cell lung cancer (Bell and Seetharam, Int. J. Cancer (1976) 18:605-611; and oat **cell tumor** (Bernal and Speak, Cancer Res. (1984) 44:265-270. See also, DeSchryver-Keckemetri et al., Lab. Invest. (1979) 41:432-436 and Veltri et al.,. . .

SUMMARY:

BSUM(7)

Several different tumor-associated antigens expressed by non-lung **cancer cells** have previously been described as glycoconjugants. See, Hakomori and Kannagi, J. Nat. Cancer Inst. (1983) 71:231-251; Feizi (1984), in Genes and Antigens in **Cancer Cells**--The Monoclonal Antibody Approach; Contributions to Oncology, Vol. 19, Reithmuller et al., eds. (Kager, Basel) pp. 51-63; Ginsburg et al., ibid.,. . . Natl. Acad. Sci. USA (1980) 77:6114-6118; Bumol and Reisfeld, ibid. (1982) 79:1245-1249; Hellstrom et al. in Genes and Antigens in **Cancer Cells**--The Monoclonal Anti-body Approach; Contributions to Oncology, Vol. 19, Reithmuller et al., eds. (Kager, Basel) pp. 121-131; and Atkinson et al.,. . .

SUMMARY:

BSUM(21)

The polysaccharide epitopes may be characterized as being present in glycoproteins released by human lung **cancer cells**, which polysaccharide binds specifically to the monoclonal antibody 43-9F and is of less than about 250 kDal, generally less than. . .

SUMMARY:

BSUM(24)

The . . . of containing the antigen. Protocols involve a wide variety of labels, which labels include radionuclides, enzymes, fluorescers, fluorescer-quencher combinations, chemiluminescers, **magnetic particles**, and the like. These labels may be directly conjugated to the monoclonal antibody through a variety of covalently bonded linking. . .

DETDESC:

DETD(14)

Human . . . less than that in serum containing media. A human small cell lung carcinoma line RH-SCC-L10 was similarly maintained. The human **cancer cell** line V-266, a human myeloma line, 1-11D, and a hybridoma from human lymphocyte fusion with RH-L4 (B-lymphoma, Olsson, et al.,. . .

DETDESC:

DETD(16)

Tumor . . . of the material was homogenized after isolation of the cortical part of the tumor that normally contains most of the **tumor cells**, frozen in RPMI-1640 containing 30% FCS with 10% dimethyl sulfoxide (DMSO), and stored in liquid nitrogen. The leukemia samples were. . .

DETDESC:

DETD(35)

For testing reactivity of **tumor cells** with the 43- 9F antibody by ELISA methods, Triton X-100 extracts were prepared from tumors and wells of 96 well. . .

DETDESC:

DETD(40)

Mice . . . cells subsequently fused with a HAT-sensitive mouse myeloma cell line (X63-Ag8.6.5.3). Hybridoma supernatants were screened for reactivity to the lung **tumor cells** by cell-binding ELISA (Olsson, Cancer Metastasis Rev. (1983) 2:153-163)

DETDESC:

DETD(41)

EL . . . as a first step and FITC-conjugated rabbit anti-mouse Ig (Dako, Denmark) as a second step. Mab reactive with the lung **tumor cell** line was subsequently tested against a panel of normal and neoplastic human cells, including lymphocytes, granulocytes, monocytes, erythrocytes, thymocytes, bone. . . cells, lymphoma cells, myeloma cells, carcinoma cells and melanoma cells. Three Mabs, designated 2-4D, 2-9F, and 3-5B, reacted with lung **tumor cells**, but none with any of the other cell types. These antibodies were therefore assumed to detect lung tumor-associated antigens. These. . .

DETDESC:

DETD(44)

Triton . . . different squamous lung carcinomas, whereas specific binding could not be detected in extracts from normal human cell types or other **cancer cell** lines. The 43- 9F negative cell types include those derived from other types of human lung **cancer cells**, from normal lung cells as well as cell lines derived from malignant neoplasms of other tissues and some other normal. . .

DETDESC:

DETD(45)

For . . . (other than RH-SLC-cells) were completely negative for reaction with the 43- 9F-antibody. For example, normal lung tissue or small cell **carcinoma** cells gave no **detectable** reaction and quantitative comparison of the dot blots permitted the estimation that the amount of 43- 9F antigen in these. . .

DETDESC:

DETD(47)

The . . . than that present in one cell. The dot-blot assay seems superior to other available methods to detect minute amounts of **tumor cells** in otherwise normal tissues and could be useful to detect micrometastatic lesions.

DETDESC:

DETD(49)

Large . . . in the culture medium of growing RH-SLC-L11 cells. The amount is not significantly different from that observed with other lung

tumor cells such as small cell lung carcinomas. Dot-blot analysis revealed that the 43- 9F epitope is present on at least a. . .

CLAIMS:

CLMS(10)

10. An isolated, purified polysaccharide characterized as being present in glycoproteins released by human squamous lung **cancer cells**, said glycoproteins being of less than about 250kDal, and binding specifically to a monoclonal antibody according to claim 9.

CLAIMS:

CLMS(12)

12. . . . 50kDal to about 1mDal capable of binding to a monoclonal antibody according to claim 9, derived from human squamous lung **cancer cells** and substantially free of other human squamous lung **cancer cell** glycoproteins and proteins.

CLAIMS:

CLMS(20)

20. . . .
said endogenous antibodies; and
detecting the formation of immune complexes as indicative of the presence or prior presence of squamous lung **cancer cells**.

US PAT NO: 4,857,452 [IMAGE AVAILABLE] L8: 14 of 15

SUMMARY:

BSUM(5)

The above EPO application reports results of ELISA tests of 47D10 hybridoma supernatant for reactivity with various fixed normal and **tumor cell** lines as well as results of ELISA tests of purified 47D10 MAb with live cells of the same normal and. . .

SUMMARY:

BSUM(6)

The . . . antibody. Normal tissues, pancreas tissue with pancreatitis, breast tissue with fibrocystic disease and ovarian cystadenomas did not react. Metastatic pancreatic **tumor cells** were detected in lymph nodes by the antibody.

SUMMARY:

BSUM(7)

It is stated in the EPO application that 47D10 MAb is useful in the diagnosis of primary and metastatic pancreatic **tumor cells** by conventional in vivo diagnostic methods and also by conventional in vitro diagnostic procedures such as the assay of human. . .

SUMMARY:

BSUM(9)

Serum . . . against human milkfat globule membrane. PCT Publication Number WO 85/02411 reports a monoclonal antibody 3 E1-2 raised against

ductal breast **carcinoma** cells which **detects** an antigen present in elevated levels in the serum of patients with carcinoma of the breast. EPO Publication Number 160446 reports a 330 Kd antigen which is shed by breast **cancer cells**, monoclonal antibodies 21DD5 and 21DD7 to the antigen raised against breast carcinoma cells, and use of the monoclonals in a. . .

SUMMARY:

BSUM(10)

Herlyn . . . 14 raised against colon carcinoma cell lines and their use in a serum assay to detect colorectal, gastric and pancreatic **carcinoma**. The antigen **detected** by two of these antibodies is reported to be a monosialoganglioside. Haglund et al., Br. J. Cancer, 53, 197-202 (1986). . . cancer. EPO publication Number 171,083 discloses monoclonal antibodies KMO1 and KMO2 raised against a 700-1,500 Kd fraction of a colon **cancer cell** line, and their use in a serum assay to detect pancreas, colon and liver cancer.

DETDESC:

DETD(2)

A human **tumor cell** line which expresses high amounts of the 47D10 antigen, is grown to confluency in tissue culture bottles. The cells are. . .

DETDESC:

DETD(3)

To . . . mixture of serum and MAb are transferred to a second microtiter plate which has been coated with 350 ng/well of **tumor cell** membranes (prepared as described above). After an incubation of one hour at 37.degree. C., the wells are washed three times. . .

DETDESC:

DETD(10)

A . . . antigen, such as a lecithin, to a solid support. Examples of solid supports are wells of a microtiter plate, polystyrene **beads**, or **magnetic beads**. The MAb or lectin on the solid support can be used to "capture" serum antigens which are subsequently detected by. . .

US PAT NO: 4,752,569 [IMAGE AVAILABLE] L8: 15 of 15

SUMMARY:

BSUM(8)

The . . . 516:97-127; Glick, Biochemistry (1979) 18:2525-2532; and Yogeeswaran and Tao, Biochem. Biophys. Res. Commun. (1980) 95:1452-1460. Many monoclonal antibodies raised against **cancer cells** have been reported as having their main activity against terminal carbohydrate structures such as sialylated Lewis.sup.a (Magnani et al., J.. . .

SUMMARY:

BSUM(20)

The . . . enzyme substrates and inhibitors; enzymes, such as horseradish peroxidase, glucose oxidase, glucose-6-phosphate

dehydrogenase, acetylcholinesterase, etc.; particles, e.g., dextran, agarose, metal **particles, magnetic particles**, polystyrene **particles**, etc. or the like. Methods for conjugating haptens to the various labels have been extensively described in the literature, see,. . .

SUMMARY:

BSUM(33)

Cell lines. Stomach **cancer cell** line (MKN1, MKN28, MKN45 and MKN74 established by Dr. H. Hojo and KATO-III established by Dr. M. Sekiguchi) were obtained. . .

SUMMARY:

BSUM(57)

Reactivity Against Various Solid **Tumor Cell** Lines

SUMMARY:

BSUM(58)

Thirty-four various **tumor cell** lines were examined for reactivity by microcytotoxicity, immunofluorescence, and immunoperoxidase staining as shown below in Table 2. CSLEX1 yielded positive. . .

SUMMARY:

BSUM(59)

TABLE 2

Reactivity of Monoclonal Antibody CSLEX1 Against Solid **Tumor Cell** Lines by Cytotoxicity/Immunofluorescence/Immunoperoxidase

Cell Line Origin	Cytotoxicity	Immuno-fluorescence	Immuno-peroxidase
Stomach			
KATO-III			
Signet. . .			

SUMMARY:

BSUM(62)

Seventy-four various tumor tissues tested are shown in Table 4. Surprisingly, the antigen recognized by CSLEX1 antibody could be **detected** in many **carcinomas** - 16 of 17 stomach adenocarcinomas, 13 of 17 colon adenocarcinomas, 10 of 16 lung tumors, 2 of 4 esophagus. . . tissues by CSLEX1 was observed in adenocarcinomas such as stomach, colon, and lung without regard to differentiating grade of the **cancer cells**. Positive staining was also observed in some squamous cell carcinoma samples. The CSLEX1 antibody reacted with 50 of 74 (68%). . .

US PAT NO: 5,019,497 [IMAGE AVAILABLE] L10: 12 of 14

SUMMARY:

BSUM(3)

Cancer cells synthesize unusual and sometimes highly specific proteins and glycolipids that in many cases have been identified as fetal or embryonic macromolecules apparently produced in the **cancer cell** after either aberrant activation or failure to deactivate genes normally silent in differentiated cells. Some of these gene-products may influence the abnormal proliferative properties of the **cancer cells**. Sensitive methods are needed for identifying the unusual cellular compounds with high tumor specificity, because they may provide signals for. . .

SUMMARY:

BSUM(6)

Olsson et al., Cancer (1984) 54:1757-1765 report monoclonal antibodies for lung carcinoma. Antisera and monoclonal antibodies with reactivity to human lung **cancer cells** have been described by Kelly and Levy, Br. J. Cancer (1977) 35:828-833; Cuttita et al., Proc. Natl. Acad. Sci. USA. . . of the subtypes of lung cancer: small cell lung cancer (Bell and Seetharam, Int. J. Cancer (1976) 18:605-611; and oat **cell tumor** (Bernal and Speak, Cancer Res. (1984) 44:265-270. See also, DeSchryver-Keckemetri et al., Lab. Invest. (1979) 41:432-436 and Veltri et al.,. . .

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Several different tumor-associated antigens expressed by non-lung **cancer cells** have previously been described as glycoconjugants. See, Hakomori and Kannagi, J. Nat. Cancer Inst. (1983) 71:231-251; Feizi (1984), in Genes and Antigens in **Cancer Cells**--The Monoclonal Antibody Approach; Contributions to Oncology, Vol. 19, Reithmuller et al., eds. (Kager, Basel) pp. 51-63; Ginsburg et al., ibid.,. . . Natl. Acad. Sci. USA (1980) 77:6114-6118; Bumol and Reisfeld, ibid. (1982) 79:1245-1249; Hellstrom et al. in Genes and Antigens in **Cancer Cells**--The Monoclonal Anti-body Approach; Contributions to Oncology, Vol. 19, Reithmuller et al., eds. (Kager, Basel) pp. 121-131; and Atkinson et al.,. . .

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DETDESC:

DETD(14)

Human . . . less than that in serum containing media. A human small cell lung carcinoma line RH-SCC-L10 was similarly maintained. The human **cancer cell** line V-266, a human myeloma line, 1-11D, and a hybridoma from human lymphocyte fusion with RH-L4 (B-lymphoma, Olsson, et al.,. . .

DETDESC:

DETD(16)

Tumor . . . of the material was homogenized after isolation of the cortical part of the tumor that normally contains most of the **tumor cells**, frozen in RPMI-1640 containing 30% FCS with 10% dimethyl sulfoxide (DMSO), and stored in liquid nitrogen. The leukemia samples were. . .

DETDESC:

DETD(28)

When . . . When unlabeled monoclonal antibody was used, it was detected by incubating the washed sheet with a 1:500 dilution of a **peroxidase** conjugated rabbit-anti-mouse IgG light chain (DAKO) in PBS Tween plus 30% FCS. After washing the sheet, the **peroxidase** staining was developed with diaminobenzidine.

DETDESC:

DETD(35)

For testing reactivity of **tumor cells** with the 43- 9F antibody by ELISA methods, Triton X-100 extracts were prepared from tumors and wells of 96 well plates coated with extract corresponding to roughly 10.sup.5 -10.sup.6 cells, as described above. The monoclonal 43- 9F antibody was **peroxidase** conjugated and the ELISA assay carried out as a one-step procedure. The plates were incubated with the specific antibody (.about.100ng/well). . . hr at room temperature and 1 hr at 37.degree. C., washed, and incubated for 2 hr at room temperature with **peroxidase** conjugated 43- 9F. The reading of the test was done as described above.

DETDESC:

DETD(40)

Mice . . . cells subsequently fused with a HAT-sensitive mouse myeloma cell line (X63-Ag8.6.5.3). Hybridoma supernatants were screened for reactivity to the lung **tumor cells** by cell-binding ELISA (Olsson, Cancer Metastasis Rev. (1983) 2:153-163)

DETDESC:

DETD(41)

EL . . . as a first step and FITC-conjugated rabbit anti-mouse Ig (Dako, Denmark) as a second step. Mab reactive with the lung **tumor cell** line was subsequently tested against a panel of normal and neoplastic human cells, including lymphocytes, granulocytes, monocytes, erythrocytes, thymocytes, bone. . . cells, lymphoma cells, myeloma cells, carcinoma cells and melanoma cells. Three Mabs, designated 2-4D, 2-9F, and 3-5B, reacted with lung **tumor cells**, but none with any of the other cell types. These antibodies were therefore assumed to detect lung tumor-associated antigens. These. . .

DETDESC:

DETD(44)

Triton . . . different squamous lung carcinomas, whereas specific binding could not be detected in extracts from normal human cell types or other **cancer cell** lines. The 43- 9F negative cell types include those derived from other types of human lung **cancer cells**, from normal lung cells as well as cell lines derived from malignant neoplasms of other tissues and some other normal. . .

DETDESC:

DETD(45)

For . . . (other than RH-SLC-cells) were completely negative for reaction with the 43- 9F-antibody. For example, normal lung tissue or small cell **carcinoma** cells gave no **detectable** reaction and quantitative comparison of the dot blots permitted the estimation that the amount of 43- 9F antigen in these. . .

DETDESC:

DETD(47)

The . . . than that present in one cell. The dot-blot assay seems superior to other available methods to detect minute amounts of **tumor cells** in otherwise normal tissues and could be useful to detect micrometastatic lesions.

DETDESC:

DETD(49)

Large . . . in the culture medium of growing RH-SLC-L11 cells. The amount is not significantly different from that observed with other lung **tumor cells** such as small cell lung carcinomas. Dot-blot analysis revealed that the 43- 9F epitope is present on at least a. . .

CLAIMS:

CLMS(10)

10. An isolated, purified polysaccharide characterized as being present in glycoproteins released by human squamous lung **cancer cells**, said glycoproteins being of less than about 250kDal, and binding specifically to a monoclonal antibody according to claim 9.

CLAIMS:

CLMS(12)

12. . . . 50kDal to about 1mDal capable of binding to a monoclonal antibody according to claim 9, derived from human squamous lung **cancer cells** and substantially free of other human squamous lung **cancer cell** glycoproteins and proteins.

CLAIMS:

CLMS(20)

20. . . .
said endogenous antibodies; and
detecting the formation of immune complexes as indicative of the presence or prior presence of squamous lung **cancer cells**.

US PAT NO: 4,857,452 [IMAGE AVAILABLE] L10: 13 of 14

SUMMARY:

BSUM(5)

The above EPO application reports results of ELISA tests of 47D10 hybridoma supernatant for reactivity with various fixed normal and **tumor cell** lines as well as results of ELISA tests of purified 47D10 MAb with live cells of the same normal and. . .

SUMMARY:

BSUM(6)

The . . . antibody. Normal tissues, pancreas tissue with pancreatitis, breast tissue with fibrocystic disease and ovarian cystadenomas did not react. Metastatic pancreatic **tumor cells** were detected in lymph nodes by the antibody.

SUMMARY:

BSUM(7)

It is stated in the EPO application that 47D10 MAb is useful in the diagnosis of primary and metastatic pancreatic **tumor cells** by conventional in vivo diagnostic methods and also by conventional in vitro diagnostic procedures such as the assay of human. . .

SUMMARY:

BSUM(9)

Serum . . . against human milkfat globule membrane. PCT Publication Number WO 85/02411 reports a monoclonal antibody 3 El-2 raised against ductal breast **carcinoma** cells which **detects** an antigen present in elevated levels in the serum of patients with carcinoma of the breast. EPO Publication Number 160446 reports a 330 Kd antigen which is shed by breast **cancer cells**, monoclonal antibodies 21DD5 and 21DD7 to the antigen raised against breast carcinoma cells, and use of the monoclonals in a. . .

SUMMARY:

BSUM(10)

Herlyn . . . 14 raised against colon carcinoma cell lines and their use in a serum assay to detect colorectal, gastric and pancreatic **carcinoma**. The antigen **detected** by two of these antibodies is reported to be a monosialoganglioside. Haglund et al., Br. J. Cancer, 53, 197-202 (1986). . . cancer. EPO publication Number 171,083 discloses

monoclonal antibodies KMO1 and KMO2 raised against a 700-1,500 Kd fraction of a colon **cancer cell** line, and their use in a serum assay to detect pancreas, colon and liver cancer.

DETDESC:

DETD(2)

A human **tumor cell** line which expresses high amounts of the 47D10 antigen, is grown to confluency in tissue culture bottles. The cells are. . .

DETDESC:

DETD(3)

To . . . mixture of serum and MAb are transferred to a second microtiter plate which has been coated with 350 ng/well of **tumor cell** membranes (prepared as described above). After an incubation of one hour at 37.degree. C., the wells are washed three times. . . time with PBS. To detect the bound 47D 10 MAb, 50 .mu.l of goat anti-mouse IgG antibody conjugated to horseradish **peroxidase** (GAMHRP), diluted 1:15,000 in PBS-1% BSA, are added to each well. The plate is incubated for 60 min. at 37.degree.. . .

DETDESC:

DETD(10)

A . . . antigen, such as a lecithin, to a solid support. Examples of solid supports are wells of a microtiter plate, polystyrene **beads**, or **magnetic beads**. The MAb or lectin on the solid support can be used to "capture" serum antigens which are subsequently detected by. . .

US PAT NO: 4,752,569 [IMAGE AVAILABLE] L10: 14 of 14

SUMMARY:

BSUM(8)

The . . . 516:97-127; Glick, Biochemistry (1979) 18:2525-2532; and Yogeeswaran and Tao, Biochem. Biophys. Res. Commun. (1980) 95:1452-1460. Many monoclonal antibodies raised against **cancer cells** have been reported as having their main activity against terminal carbohydrate structures such as sialylated Lewis.sup.a (Magnani et al., J.. . .

SUMMARY:

BSUM(20)

The . . . .sup.131 I; fluorescers, e.g., fluorescein, phycobiliproteins, rare earth chelates, dansyl, rhodamine, etc.; enzyme substrates and inhibitors; enzymes, such as horseradish **peroxidase**, glucose oxidase, glucose-6-phosphate dehydrogenase, acetylcholinesterase, etc.; particles, e.g., dextran, agarose, metal **particles**, **magnetic particles**, polystyrene **particles**, etc. or the like. Methods for conjugating haptens to the various labels have been extensively described in the literature, see,. . .

SUMMARY:

BSUM(33)

Cell lines. Stomach **cancer cell** line (MKN1, MKN28, MKN45 and

MKN74 established by Dr. H. Hojo and KATO-III established by Dr. M. Sekiguchi) were obtained. . .

SUMMARY:

BSUM(36)

For . . . added and incubated for 2 hr at 37.degree. C. After washing 3 times (with PBS-0.05% Tween 20.TM.), 5 .mu.l of **peroxidase**-labeled goat antimouse Ig (IgG+IgM) (KPL Laboratories) were allowed to react for 1 hr at 37.degree. C. After washing 5 times,. . .

SUMMARY:

BSUM(42)

Normal . . . hr at room temperature. Five to ten .mu.g/ml mouse myeloma IgM were used as negative controls. After washing in PBS, **peroxidase** conjugated F(ab').sub.2 of goat antimouse IgG+IgM (KPL Laboratories) diluted 1:100 was added to the tissue section for 45 min at. . .

SUMMARY:

BSUM(44)

To . . . reactions were performed at 37.degree. C. for one hour. Following the enzymatic reaction, an ELISA was performed using the enzyme **peroxidase** and 5 mM sodium periodate incubated at 4.degree. C. for one hour.

SUMMARY:

BSUM(57)

Reactivity Against Various Solid **Tumor Cell** Lines

SUMMARY:

BSUM(58)

Thirty-four various **tumor cell** lines were examined for reactivity by microcytotoxicity, immunofluorescence, and immunoperoxidase staining as shown below in Table 2. CSLEX1 yielded positive. . .

SUMMARY:

BSUM(59)

TABLE 2

Reactivity of Monoclonal Antibody CSLEX1 Against Solid **Tumor Cell** Lines by Cytotoxicity/Immunofluorescence/Immunoperoxidase

Cell Line Origin	Cytotoxicity	Immuno-fluorescence	Immuno-**peroxidase**
Stomach			
KATO-III			
Signet ring cell carcinoma			

+ (1:10.sup.4)

+ +

MKN28 Adenocarcinoma (well) *

N.T.* + +. . .

SUMMARY:

BSUM(62)

Seventy-four various tumor tissues tested are shown in Table 4. Surprisingly, the antigen recognized by CSLEX1 antibody could be detected in many carcinomas - 16 of 17 stomach adenocarcinomas, 13 of 17 colon adenocarcinomas, 10 of 16 lung tumors, 2 of 4 esophagus. . . tissues by CSLEX1 was observed in adenocarcinomas such as stomach, colon, and lung without regard to differentiating grade of the cancer cells. Positive staining was also observed in some squamous cell carcinoma samples. The CSLEX1 antibody reacted with 50 of 74 (68%). . .